Abstract:
This article reports a well-powered age-related macular degeneration (AMD) case-control association study in the HMCN1 gene, showing that common variants do not account for a substantial proportion of AMD cases. Thus, the consistent linkage peak observed by several genome-wide linkage scans within the 1q32 region is unlikely to be attributed to polymorphisms at the HMCN1 locus. In addition, the analysis provides comprehensive data suggesting that low-frequency variants encoding possible functional amino acid polymorphisms in the HMCN1 gene may not contribute substantially to disease, although HMCN1 mutations may still confer disease susceptibility in a small subset of patients. Interestingly, the HMCN1 p.Gln5346Arg mutation, which is thought to be a causal mutation in a large AMD pedigree segregating the disease as a single-gene trait, appears to occur in our control cohort as a low-frequency polymorphism with an allele frequency of approximately 0.0026.